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09/147,052	04/05/99	SAITOH	S 981167

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EXAMINER	
HINES,J	
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary	Application No. 09/147,052	Applicant(s) SAITOH ET AL.	
	Examiner Ja-Na A Hines	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *August 2, 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *20-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *20-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Amendment Entry

1. Amendments filed on August 2, 2001 have been entered. Claims 2-11 and 15-19 have been canceled. Claims 20-26 have been added. Claims 20-26 are under consideration in the office action.

Withdrawal of Rejections

2. Claim 18 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

3. Claim 19 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated fusion protein comprising SEQ ID NO:2 and 4, does not reasonably provide enablement for a fusion protein comprise a polypeptide causing an antibody-antigen reactions and having a epitope and a polypeptide having a epitope of Herpesvirus outer membrane protein which has a sequence 90% homologous to the native Herpesvirus outer membrane protein is withdrawn in view of applicants amendments.

4. Claim 17 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of applicants amendments.

5. Claims 2-11 and 15-19 objected to because of the following informalities: In claim 18 Mg should be designated as an acronym for *M. gallisepticum* is withdrawn in view of applicants amendments.

6. Claim 16 objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependency on any of claims 2-8 and 18.

Response to Arguments

7. Applicant's arguments filed August 2, 2001 have been fully considered but they are not persuasive.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. The rejection of claims 20-26 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained. The written description in claim 20 sets forth that the fusion protein comprises an antigenic protein derived from *M. gallisepticum* causing an antibody-antigen reaction and a signal polypeptide of Herpesvirus outer membrane protein, therefore the written description is not commensurate in scope with the claims.

Applicant urges that the specification teaches a variety of signal sequences that are detectable at the carboxyl or amino terminus, and is exemplified in amino acids 1-63

of SEQ ID NO:2. However, a skilled artisan cannot envision the detailed structure of a signal polypeptide of Herpesvirus outer membrane, thus conception is not achieved until reduction to practice has occurred. The description of the signal polypeptide is not limited to the signal sequence of SEQ ID NO:2.

Applicant asserts that the epitope of the antigenic protein region varies for every protein yet the method for determining the epitope region is disclosed in the specification. However, it is the examiner's position that written description of the antigenic protein is lacking and not clearly stated if the antigenic protein varies so much regardless of the complexity or simplicity of the method of isolation. There are many known epitopes and antigenic regions of the Mg polypeptide, and the claims as written do not clearly describe which region applicant is referring to. An adequate description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The court *In The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), stated that an adequate written description of a DNA or polypeptides comprising epitopes...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention". Therefore the rejection is maintained.

9. The rejection of claim 26 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is maintained. Claim 26 is directed to a recombinant live vaccine for anti-fowl Mg infection comprising fusion proteins as effective ingredients against subsequent infection with *Mycoplasma gallisepticum*. However, the instant

specification fails to provide any experiments that show that such a vaccine would be effective in protecting against *Mycoplasma gallisepticum.*

Applicant argues that examples 5-6 report comparative experiments on the antibody-inducing capabilities and resistance to challenge with Mg using the vaccine of claim 26, therefore a person of ordinary skill would find guidance and an expectation of success without requiring undue experimentation. Example 6 teaches a challenge test wherein the results reveal that the 40K-S and 40K-C vaccines could be effective vaccines. However, claim 26 is not limited to the 40K-S or –C vaccines but rather to a more generic version. Because the vaccine art is highly unpredictable and the instant specification fails to provide any information that any fusion protein providing immunity from a *Mycoplasma gallisepticum* infection the rejection is maintained. There are no protocols provided which demonstrate which fusion proteins would be effective in immunization, nor are there any protocols detailing the amount of fusion protein which is needed to mount a sufficient immune response. The art is replete with instances where even well characterized antigens that induce an in vitro neutralizing antibody response fail to elicit in vivo protective immunity. Therefore, it would require undue experimentation given the fact that the specification is completely lacking in teachings as to fusion proteins with the claimed characteristics.

10. The rejection of claims 20-26 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained. Applicants argue that the specification details a description of the derived Mg polypeptide, herpes virus, and Marek's disease. However the claims are indefinite. The term "derived" does not provide the character or properties from the source that are to be retained in the final product, e.g., paper is

derived from wood but is very different from wood. The phrase "derived from" should be changed to "isolated from". The specification does not teach how to make additional derivatives nor do the claims recite what characteristics are needed to determine whether an unknown polypeptide could be considered a derivative polypeptide. The specification does not disclose a definition or limitations for any derived polypeptide, nor does the specification teach a requisite amount of retained qualities needed or characteristics necessary to determine derivative polypeptides. Therefore, the rejection is maintained.

11. The rejection of claim 26 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained. Claim 26 recites DNA coding for the fusion protein, however no specific DNA sequence is recited. Applicants argue that it is submitted that the DNA sequence corresponding to many such polypeptides is known, as mentioned in the specification, or can be determined by conventional methods. However, it is examiner's position that there is no teaching of what specific nucleic acids are required in the DNA sequence to code for the fusion protein. Applicants have not stated a specific SEQ ID Number nor have they described a particular fusion protein to be encoded.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. The rejection of claims 20-24 under 35 U.S.C. 103(a) as being unpatentable over Saito et al., (WO 94/23019) in view of Yoshida et al., (Virology 1994 Vol. 200) is maintained. Applicants argue that none of the cited references teach the immunological effects in vivo.

However, it is noted that the features upon which applicant relies, such as testing antigenicity *in vivo,* are not recited in the rejected claims. Even though, antigenicity testing is not recited in the claims, Saito et al., teaches the expression with a recombinant virus of a polypeptide modified to such an extent as to exhibit an antigenicity equivalent to that of any of the above polypeptides. Thus, Saito et al., teaches antigenicity.

Applicants argue that none of the cited references teach the use of a signal sequence of gB gene derived from Marek's disease. However, Yoshida et al., clearly teach that the Marek's Disease Virus (MDV)-1 homolog of the herpes simplex virus glycoproteinB (gB) has been cloned and sequenced. Recombinant fowlpox virus (FPV) has been used to express foreign genes and to evaluate immunogenic potential wherein the data suggest that FPV recombinant is a good candidate for an MDV vaccine and that gB is an important target for the host immune response.

Therefore, the cited prior art clearly teaches these aspects of the instant claims, thus the rejection is maintained.

13. Applicants point to the experimental data reported in the declaration shows improved effects as compared to the fusion protein of Saito. The declaration purportedly teaches that inoculation with fNZ7929-67, fNZ7929-66 or fNZ2929XM1 shows better results than with the fusion protein of Saito et al., (WO 94/23019).

However, the declaration under 37 CFR 1.132 filed June 27, 2000 is insufficient to overcome the rejection of claims 16-17 because the Declaration does not teach the specific vaccine discussed in the claims. The claims are drawn to a fusion protein as recited in the claims and not the fusion proteins, fNZ7929-67, fNZ7929-66 or fNZ2929XM1. Therefore the statement that the recited fusion proteins perform better is not commensurate with the scope of the claims, thus the declaration is unpersuasive.

14. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, no more then routine skill would have been required to use the signal polypeptide derived Herpes outer membrane protein from Yoshida et al., (Virology 1994 Vol. 200) with the fusion protein comprising an outer membrane protein that infects birds and vaccine of Saito et al., (WO 94/23019) because Yoshida et al., teach that the FPV recombinant express the gB-1 gene which can elicit neutralizing antibody and fully protect chickens against challenges with virulent strains of MDV; the FPV recombinant is a good candidate for an MDV vaccine; and that gB is an important target for the host immune response thus providing motivation for inclusion.

One of ordinary skill in the art would have clearly been motivated to use the fused polypeptide comprising a signal polypeptide and exchange the signal polypeptide of Saito et al., ~~which~~ with the signal polypeptide of Yoshida et al., because of the many beneficial effects Yoshida et al., teach. One having ordinary skill in the art would have been motivated to make such a change as a mere alternative and functionally equivalent polypeptide since only the expected results are taught. The use of alternative signal polypeptides would have been desirable to those of ordinary skill in the art based on the fact that gB-1 gene elicits neutralizing antibody; fully protects chickens against virulent strains of MDV and it is a good candidate for an MDV vaccine. Therefore, the rejection is maintained.

15. The rejection of claims 25-26 under 35 U.S.C. 103(a) as being unpatentable over Saito et al., (WO 94/23019) in view of Yoshida et al., (Virology 1994 Vol. 200) and further in view of Yangida et al., is maintained. Applicants argue that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art.

In this case, Saito et al., (WO 94/23019) and Yoshida et al., (Virology 1994 Vol. 200) have been discussed above. Yangida et al., teach recombinant Avipox virus having all or part of cDNA for Newcastle disease virus derived fused proteins. Thus, it would have been obvious at the time of applicants invention to use the recombinant

Avipox virus with exogenous DNA as taught by Yangida et al, with the fusion polypeptide of Saito et al., (WO 94/23019) in view of Yoshida et al., (Virology 1994 Vol. 200) because Yangida et al., teach that recombinant Avipoxvirus genes are effective as vaccine and can prevent infections of Avipoxvirus.

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is (703) 305-0487. The examiner can normally be reached on Monday through Thursday from 6:30am to 4:00pm. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Ja-Na Hines

October 10, 2001

LYNETTE R. F. SMITH
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